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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,507	12/08/2000	Hong Wang	4810-56910	2417

7590 11/17/2004

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EXAMINER	
COLLINS, CYNTHIA E	
ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,507	WANG ET AL.	
	Examiner	Art Unit	
	Cynthia Collins	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *September 7, 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-9,11-15,18,20-22 and 27-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,11-15,18,20-22 and 27-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The Appeal Brief filed September 7, 2004 has been entered.

Claims 10, 16-17, 19 and 23-26 are cancelled.

The finality of the action mailed November 5, 2003 is hereby withdrawn.

Claims 1-9, 11-15, 18, 20-22 and 27-33 are pending and are examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

All previous objections and rejections not set forth below have been withdrawn.

Claim Rejections - 35 USC § 112

Claims 1-9, 11-15, 18, 20-22, 27, 30 and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the office action mailed November 5, 2003, and for the additional reasons set forth below.

Applicant's arguments filed September 7, 2004, have been fully considered but they are not persuasive.

As a preliminary matter, Applicants maintain that the Examiner has not established a prima facie case as required by MPEP § 2163(III)(A), by providing reasons why a skilled person would not recognize that the Applicants had possession of the invention. At most, the Examiner has provided general allegations of unpredictability, which is not sufficient - as stated explicitly in MPEP 2163.04(1). Absent a prima facie

case, Applicants maintain that the Examiner has not met the burden in this case to make a rejection of these claims for alleged failure of written description. (brief page 4)

As previously stated at page 4 of the office action mailed November 5, 2003, the Examiner reiterates that the outstanding written description rejection was not predicated on unpredictability. The outstanding written description rejection was predicated on the failure to describe a substantial portion of the genus that comprises a nucleic acid encoding a plant cyclin-dependent kinase inhibitor polypeptide that functions to modify development when expressed in a transformed plant, and on the failure to describe a substantial portion of the genus comprises a nucleic acid encoding a heterologous cyclin-dependent kinase inhibitor polypeptide that functions to modify development when expressed in a transformed plant (page 3 of the office action mailed November 10, 2002; pages 3-4 of the office action mailed November 5, 2003).

Applicants also submit that, although the present claims have been restricted to claiming a single species in response to the Restriction Requirement, a full spectrum of plant cyclin-dependent kinase (CDK) inhibitors is in fact disclosed: ICK2, ICN2, ICN6, and ICN7. Applicants further point out that a consensus sequence is provided in Figure 7. Applicants accordingly submit that the Guidelines do not dictate that the present claims contravene § 112. (brief pages 4-5)

The Examiner maintains that because the cyclin-dependent kinase inhibitor polypeptides of ICK2, ICN2, ICN6, and ICN7 were all obtained from a single plant species (*Arabidopsis thaliana*), they do not constitutive a representative number of species describing a broad genus of cyclin-dependent kinase inhibitor polypeptides

obtained any plant species, or the broader genus of heterologous cyclin-dependent kinase inhibitor polypeptides obtained from any organism. The Examiner also maintains that because the disclosed cyclin-dependent kinase inhibitor polypeptides all correspond to a single class of cyclin-dependent kinase inhibitor polypeptides (Cip/Kip), they do not constitutive a representative number of species describing all classes of plant cyclin-dependent kinase inhibitor polypeptides, or all classes of heterologous cyclin-dependent kinase inhibitor polypeptides. The Examiner further maintains that none of the rejected claims require that the encoded cyclin-dependent kinase inhibitor polypeptides comprise the disclosed consensus sequence.

In this regard the Examiner notes that the prior art discloses a number of structurally and functionally distinct classes of proteins that can inhibit cyclin-dependent kinases. See, for example, Peter M (The regulation of cyclin-dependent kinase inhibitors (CKIs). Prog Cell Cycle Res. 1997;3:99-108), who teaches that two different classes of proteins are known to inhibit the protein kinase activity of CDKs by directly binding to the CDK complex, the Cip/Kip class of proteins that bind CDK complexes through a conserved N-terminal domain thus inhibiting complexes in which Cdk2, Cdk4 and Cdk6 are associated with A-, D- and E-type cyclins, and the Ink class of proteins that are characterized by ankyrin repeats and that specifically inhibit Cdk4 and Cdk6 complexes (page 99 column 1 first paragraph).

See also, for example, Sun Y et al (Characterization of maize (*Zea mays* L.) Wee1 and its activity in developing endosperm. Proc Natl Acad Sci U S A. 1999 Mar 30;96(7):4180-5), who teach another class of proteins known to inhibit the protein kinase activity of CDKs, the class of proteins exemplified by Wee1, Mik1 and Myt1 that inhibit

CDK activity by phosphorylating CDKS at threonine 14 and/or tyrosine 15 of their catalytic subunits (page 4180 column 1 through column 2 first paragraph; page 4182 Figure 2).

In this regard the Examiner also notes that the prior art discloses that the kingdom from which plant cyclin-dependent kinase inhibitor polypeptides would be obtained comprises an enormous number of different species, and the combined eukaryotic kingdoms from which heterologous cyclin-dependent kinase inhibitor polypeptides would be obtained comprises even more.

See, for example, Margulis M (Biodiversity: molecular biological domains, symbiosis and kingdom origins. Biosystems. 1992;27(1):39-51), who teaches that the plant kingdom comprises an estimated 400,000 species, and that the combined eukaryotic kingdoms (plant, animal fungal and protist) comprise an estimated 30,720,000 species (page 40 Table 1).

In the instant case the disclosure of cyclin-dependent kinase inhibitor polypeptides corresponding to a single class of cyclin-dependent kinase inhibitor polypeptides (Cip/Kip) obtained from only two species of plants does not constitutive a representative number of species describing all classes of plant cyclin-dependent kinase inhibitor polypeptides, or all classes of heterologous cyclin-dependent kinase inhibitor polypeptides.

Applicants additionally note the Guidelines state that, for each claim drawn to a genus, the written description requirement may be satisfied through sufficient description of a representative number of species, by actual reduction to practice, reduction to

drawings, or by disclosure of relevant, identifying characteristics, and Applicants maintain that an actual reduction to practice of each and every species within a claimed genus is accordingly not a requirement of the Guidelines. Applicants also note that sequences are provided for a representative number of cyclin-dependent kinase inhibitors in the present application, illustrating an actual reduction to practice for each of these CDK inhibitors. Applicants further note that Example 18 in the Guideline Training Material is illustrative of the fact that, where there is an actual reduction to practice of even a single embodiment, a claim which encompasses a relevant genus may nevertheless be fully supported and adequately described, and Applicants also note that the fact that not every species within a genus needs to be enumerated is further emphasized in MPEP § 2163(II)(A)(3)(a)(ii). (brief page 5).

The Examiner maintains that the outstanding written description rejection is not predicated on the failure to reduce to practice each and every species within the claimed genus. The outstanding written description rejection is predicated on the failure to describe a substantial portion of the claimed genus (page 3 of the office action mailed November 10, 2002; pages 3-4 of the office action mailed November 5, 2003).

With respect to Applicants' assertion that sequences are provided for a representative number of cyclin-dependent kinase inhibitors in the present application, the Examiner maintains that the sequences disclosed (ICK1, ICK2, ICN2, ICN6, and ICN7 obtained from *Arabidopsis thaliana*, and CDKI1 obtained from *Chenopodium rubrum*) are not representative of the genus claimed (any unspecified type of cyclin-dependent kinase inhibitor obtained from any plant species and any unspecified type of heterologous cyclin-dependent kinase inhibitor obtained from any unspecified organism).

With respect to Applicants' reference to Example 18 in the Guideline Training Material, the facts at issue in the cited example are not analogous to the facts at issue here. Example 18 is directed to a process claim (a method for producing proteins in *Neurospora crassa* mitochondria) where the novelty is in the method steps. In Example 18 an actual reduction to practice of a single embodiment of the method was said to adequately describe a claim encompassing a genus of methods for producing proteins in *Neurospora crassa* mitochondria, given the teachings of the prior art that there is no substantial variation within the genus. Here the disclosure of a limited number of species of plant cyclin-dependent kinase inhibitor polypeptides does not adequately describe a claim encompassing the use of a broad genus of plant cyclin-dependent kinase inhibitor polypeptides or heterologous cyclin-dependent kinase inhibitor polypeptides because the art does not indicate that there is no substantial variation within the claimed genus.

Applicants additionally maintain that the Examiner was mistaken in alleging that Applicants disclosed CDK inhibitors from only a single plant species, and that the specification provides nucleic acid and amino acid sequences for a representative number of cyclin-dependent kinase inhibitors from more than one plant species and genus. Applicants point out that in addition to the CDK inhibitors from *Arabidopsis thaliana*, the specification (page 35, lines 22 to page 36, line 12) describes a cDNA clone having sequence similarity with other CDK inhibitors, CDKI1 (SEQ ID NOs: 15 and 16), obtained from *Chenopodium rubrum* (see, table 2, page 36). Applicants additionally point out that an expression construct of CDKI1 was used to transform *Arabidopsis* which resulted in significant morphological changes in plant development in over one

third of the transformants, and that these results were obtained regardless of the fact that *Arabidopsis* and *Chenopodium* are phylogenetically distant species (which is noted in the specification at page 36, lines 4-12). Applicants respectfully submit that the written description requirement for a claimed genus has been fulfilled as the description clearly contains a sufficient description of CDK inhibitors from a representative number of distantly related species (and not a single plant species, as alleged by the Examiner) by actual reduction to practice. Furthermore, Applicants submit that the skilled person would recognize from the disclosure that the Applicants were in possession of the claimed genus. (brief page 6)

The Examiner acknowledges that the specification at page 35 discloses CDKI1 (SEQ ID NOs: 15 and 16), obtained from *Chenopodium rubrum*, and that the specification at page discloses the transformation of *Arabidopsis* with CDKI1. The Examiner maintains, however, that the disclosure of only one type of cyclin-dependent kinase polypeptide obtained from only two plant species does not constitutive a representative number of species describing a broad genus of any unspecified type of cyclin-dependent kinase inhibitor obtained from any plant species and any unspecified type of heterologous cyclin-dependent kinase inhibitor obtained from any unspecified organism. The Examiner further maintains that an assertion that the skilled person would recognize from the disclosure that the Applicants were in possession of the claimed genus does not substitute for a description of a representative number of species describing the broadly claimed genus, because a showing of possession alone does not satisfy the written description requirement. See *Enzo Biochem Inc. v. Gen-Probe Inc.*, 63 USPQ2d 1609, 1617:

> Application of the written description requirement, however, is not subsumed by the "possession" inquiry. A showing of "possession" is ancillary to the *statutory* mandate that "[t]he specification shall contain a written description of the invention," and that requirement is not met if, despite a showing of possession, the specification does not adequately describe the claimed invention. After all, as indicated above, one can show possession of an invention by means of an affidavit or declaration during prosecution, as one does in an interference or when one files an affidavit under 37 C.F.R. § 1.131 to antedate a reference. However, such a showing of possession alone does not cure the lack of a written description in the specification, as required by statute.

Applicants further submit that the Examiner has erred in stating that the rejected claims recite no structural limitations that identify a CDK inhibitor as ICKI, or as an *Arabidopsis* CDK inhibitor, or as a plant CDK inhibitor, or make reference to the consensus sequence of figure 7, because independent claims 1 and 27 are specifically directed to a plant cyclin-dependent kinase inhibitor polypeptide, and because independent claims 30 and 32 are directed to a nucleic acid encoding an *Arabidopsis* CDK inhibitor polypeptide (brief pages 6-7).

The Examiner maintains that the rejected claims recite no structural limitations. The names recited in claims 1-5, 15, 17, 27, 30 and 32, "plant cyclin-dependent kinase inhibitor polypeptide", "plant cyclin-dependent kinase inhibitor polypeptide homologous to ICK1", "ICK1 plant cyclin-dependent kinase inhibitor polypeptide", "cyclin-dependent kinase inhibitor polypeptide capable of inhibiting a cyclin-dependent kinase", "cyclin-dependent kinase inhibitor" and "*Arabidopsis* cyclin-dependent kinase inhibitor polypeptide", do not impart structure to the sequences recited in the claims because the named genera are not adequately described. See *University of California v. Eli Lilly,* 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997), where it states:

> naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. Thus, as we have previously held, a cDNA is not defined or described by the mere name "cDNA," even if accompanied by the name of the protein that it encodes, but requires a kind of specificity usually achieved by means of the recitation of the sequence of nucleotides that make up the cDNA. *See Fiers,* 984 F.2d at 1171, 25 USPQ2d at 1606.

With respect to the actual reduction to practice and specific phenotypic effects of the disclosed plant CDK inhibitors, Applicants submit that the specification clearly provides support that various CDK inhibitors from both *Arabidopsis* and *Chenopodium* were used to transform different plant species and that different CDK inhibitor constructs combined with the use of different constitutive and tissue specific promoters were shown to have different phenotypic effects on the transformed plants. Applicants further note that claims 2 to 5, 28, 29 and 33 all specifically recite structural limitations, in that the CDK inhibitor nucleic acid or polypeptide is either ICKI, or is homologous/shares identity with ICKI, or is represented by SEQ ID NOS: 1 or 3, or shares identity with SEQ NOS: 1 or 3, and that the Examiner, at the very least, improperly rejected these claims, as the specification clearly provides support that the Applicants were in possession of the invention as claimed in these claims. (brief pages 7-8)

With respect to dependent claims 2 to 5, the Examiner maintains that these claims do not specifically recite structural limitations as discussed above, and are therefore properly rejected. However, upon reconsideration, and in light of their recitation of specific structural limitations (SEQ ID NOS:1 and 3 and sequences having 95% sequence identity thereto), the rejection of claims 28-29, 31, and 33 is hereby withdrawn.

Claims 1-9, 11-15, 18, 20-22 and 27-33 are rejected under 35 U.S.C. 1 12, first paragraph, because the specification, while being enabling for transforming a plant with a nucleic acid of SEQ ID NO:1 encoding the *Arabidopsis* cyclin-dependent kinase inhibitor ICKI, wherein the cyclin-dependent kinase inhibitor ICKI is expressed in petal and stamen primordia to inhibit floral development, and for transforming a plant with a nucleic acid of SEQ ID NO:1 encoding the *Arabidopsis* cyclin-dependent kinase inhibitor ICKI, wherein the cyclin-dependent kinase inhibitor ICKI is expressed in leaf cells to decrease ploidy, does not reasonably provide enablement for transforming a plant with a nucleic acid encoding any unspecified type of cyclin-dependent kinase inhibitor obtained from any unspecified source, wherein the cyclin-dependent kinase inhibitor is expressed in any unspecified proliferative tissue to inhibit any unspecified aspect of development of any unspecified differentiated tissue. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims, for the reasons of record set forth in the office action mailed November 5, 2003, and for the additional reasons set forth below.

Applicant's arguments filed September 7, 2004, have been fully considered but they are not persuasive.

Applicants submit that no undue experimentation is required to practice the full scope of the invention because only routine assays are required to identify selected optimal embodiments of the claimed invention. Applicants also submit that even a large amount of experimentation may not be considered undue where such experimentation is routine. (brief page 8)

Applicants point in particular to *In re Wands* 858 F.2d 731, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) and *Genentech, Inc. v. Novo Nordisk A/S*, 108 F.3d 1361, 1365 (Fed. Cir. 1997) as setting forth factors to be used when determining whether experimentation is undue, and Applicants maintain that an analysis of several of the Wands factors supports their view that undue experimentation is not required to make and use the claimed invention to its full scope. Applicants additionally submit that the Examiner's previous assertion that that the techniques used to discriminate between embodiments would be within the abilities of the skilled artisan demonstrates that any experimentation required to practice the claimed invention is routine and not undue. (brief pages 8-9)

Further, with respect to Applicants teaching the skilled person how to discriminate between embodiments, Applicants submit that the specification provides what a modification of plant or floral development is considered to be (see tables 1 and 2, pages 30 and 36, respectively), and how to test transformants to determine if the modification has been achieved. Applicants additionally submit that the specification provides a reasonable amount of guidance with respect to disseminating between operative and inoperative embodiments, and enables the skilled person to practice any desired embodiment of the claimed invention. (brief pages 9-10)

The Examiner maintains that the outstanding enablement rejection was not predicated on the failure to provide sufficient guidance with respect to using techniques known in the art to test for the modification of plant or floral development in order to discriminate between operative and inoperative embodiments. The outstanding

enablement rejection was predicated on the failure to provide sufficient guidance with respect to which cyclin-dependent kinase inhibitors to express and which promoter sequences to use in order to obtained transgenic plants in which the development of a particular differentiated tissue is inhibited in a particular manner (pages 6-7 of the office action mailed September 10, 2002).

Such guidance is necessary because the ability of a nucleic acid encoding a plant cyclin-dependent kinase inhibitor polypeptide or a heterologous nucleic acid encoding a cyclin-dependent kinase inhibitor polypeptide to specifically modify development in a transgenic plant is unpredictable. It is unpredictable because in order to function, different types of cyclin-dependent kinase inhibitor polypeptides must interact with a variety of different types of proteins which are themselves expressed at different times and/or at different levels and/or at different locations in plants.

See, for example, Harper JW (Cyclin dependent kinase inhibitors. Cancer Surv. 1997;29:91-107), who teaches that Cip/Kip cyclin-dependent kinase inhibitor polypeptides inhibit a broader range of CDKs than do Ink4 cyclin-dependent kinase inhibitor polypeptides. Harper teaches that the Cip/Kip cyclin-dependent kinase inhibitor polypeptide p21 is a potent inhibitor of CDK2, CDK3, CDK4 and CDK6, but is a poor inhibitor of CDC2, and does not inhibit CDK7/cyclin H or CDK5/p35, whereas Ink4 cyclin-dependent kinase inhibitor polypeptides selectively inhibit only CDK4 and CDK6 (page 92 first paragraph; page 93 last paragraph).

See also, for example, Segers G et al. (The *Arabidopsis* cyclin-dependent kinase gene cdc2bAt is preferentially expressed during S and G2 phases of the cell cycle. Plant J. 1996 Oct;10(4):601-12), who teach that two different *Arabidopsis* cyclin-

dependent kinases (cdc2aAt and cdc2bAt) exhibit different levels of expression in different plant tissues and at different times during the plant cell cycle (page 602 Figure 1; page 603 Figure 2; page 604 Figure 3; page 606 Figure 4).

See additionally, for example, Dahl M et al. (The D-type alfalfa cyclin gene cycMs4 complements G1 cyclin-deficient yeast and is induced in the G1 phase of the cell cycle. Plant Cell. 1995 Nov;7(11):1847-57), who teach that two different alfalfa cyclins (cycMs4 and cycMs 2) exhibit different levels of expression in different plant tissues and at different times during the plant cell cycle (page 1815 Figure 3; page 1852 Figure 5; page 1853 Figure 6).

The ability of a nucleic acid encoding a plant cyclin-dependent kinase inhibitor polypeptide or a heterologous nucleic acid encoding a cyclin-dependent kinase inhibitor polypeptide to specifically modify development in a transgenic plant is also unpredictable because the expression of different types of cyclin-dependent kinase inhibitor polypeptides can produce different effects in vivo depending on the type and/or level of cyclin-dependent kinase inhibitor polypeptide expressed and/or the type of cell in which the cyclin-dependent kinase inhibitor polypeptide is expressed.

See, for example, Di Cunto F et al. (Inhibitory function of p21Cip1/WAF1 in differentiation of primary mouse keratinocytes independent of cell cycle control. Science. 1998 May 15;280(5366):1069-72), who teach that expression of the Cip/Kip cyclin-dependent kinase inhibitor polypeptide p21 in primary murine keratinocytes inhibited DNA synthesis and decreased expression of terminal differentiation markers, whereas expression of the Ink4 cyclin-dependent kinase inhibitor polypeptide p16 in

primary murine keratinocytes inhibited DNA synthesis but had no effect on expression of terminal differentiation markers (page 1070 Figures 1 and 2; page 1071 Figure 3).

See also, for example, Mazur X et al. (Higher productivity of growth-arrested Chinese hamster ovary cells expressing the cyclin-dependent kinase inhibitor p27. Biotechnol Prog. 1998 Sep-Oct;14(5):705-13), who teach that who teach that while transient independent expression of two different Cip/Kip cyclin-dependent kinase inhibitor polypeptides (p21 and p27) in Chinese hamster ovary cells arrested their growth, stable expression of p27 arrested growth but stable expression of p21 did not, most probably because the intracellular p21 concentrations attained during stable expression were not sufficient to promote cell cycle arrest, given that p21 is known to bind only at high concentrations to cyclin-CDK complexes to inhibit cell cycle progression (page 711 column 1second full paragraph through column 2 first paragraph).

See additionally, for example, Braun SE et al. (A positive effect of p21cip1/waf1 in the colony formation from murine myeloid progenitor cells as assessed by retroviral-mediated gene transfer. Blood Cells Mol Dis. 1998 Jun;24(2):138-48), who teach that the Cip/Kip cyclin-dependent kinase inhibitor polypeptide p21 can have a positive as well as a negative effect on cell cycle progression, as overexpression of p21 in murine bone marrow cells lines resulted in a significant increase in colony formation (page 143 Figures 3 and 4; page 144 Figure 5).

In the instant case Applicants have not provided sufficient guidance with respect to with respect to which cyclin-dependent kinase inhibitor polypeptides to express and which promoter sequences to use in order to obtained transgenic plants in which the development of a particular differentiated tissue is inhibited in a particular manner.

Absent such guidance one skilled in the art would have to test each and every promoter/cyclin-dependent kinase inhibitor polypeptide combination for its particular effect, if any, on a plant transformed therewith.

In this regard the Examiner notes that rejected claims 1-12, 15, 18, 20-22 and 28-29 impose no specific requirements with respect to the particular type of differentiated tissue affected or in what its development is inhibited. The disclosure in the specification of methods for detecting modifications of floral development and cellular ploidy does not provide sufficient guidance with respect to what other types of modifications to test for and how to detect them as claims 1-12, 15, 18, 20-22 and 28-29 require. the Examiner also notes that rejected claims 1, 6-9, 11-15, 18, 20-22 and 27 impose no specific requirements with respect to the type of plant cyclin-dependent kinase inhibitor polypeptide or heterologous cyclin-dependent kinase inhibitor polypeptide to use, and claims 1, 6-7, 13-15, 18, 20-22 and 27-33 impose no specific requirements with respect to the type of promoter to use. Given the unpredictability of the effect of expressing different types of cyclin-dependent kinase inhibitor polypeptides as set forth above, and given the breadth of the claims, the number of embodiments that would have to be tested in order to identify any additional operative embodiments is not ascertainable.

Applicants also maintain that the specification provides working examples that illustrate the effects of using multiple CDK inhibitors in more than one plant species, which species are phylogenetically diverse. Applicants submit that since the relative skill of those in the art is high, and since such artisans have the abilities necessary to employ techniques for trial and error testing to determine combinations of plant cyclin-dependent

kinase inhibitor, plant promoter, and resultant specific phenotypic effect, the technology is sufficiently predictable and the results sufficiently clear for the skilled artisan to determine, in light of Applicants' teaching which combinations work for the desired purpose. (brief page 10)

The Examiner acknowledges the disclosure of working examples that illustrate the effects of expressing more than one CDK inhibitor coding sequence in more than one plant species transformed therewith, but maintains that in addition to the previously acknowledged extensive disclosure of the effects of ICK1 expression in plants, the specification further discloses only that the expression in *Arabidopsis* of the CDKI1 or ICN2 coding sequence operably linked to the constitutive CaMV 35S promoter decreased the ploidy of plant leaf cells transformed therewith (pages 32-33), that expression in *Arabidopsis* of the CDKI1 coding sequence operably linked to an unspecified constitutive promoter resulted in transformants having significant but unspecified morphological changes in an unidentified aspect of plant development, and that expression in *Arabidopsis* of the ICN2 coding sequence operably linked to an unspecified promoter resulted in transformants having distinct but unspecified phenotypes (pages 35-36).

The Examiner maintains that the extensive disclosure of the specific effects of ICK1 expression in plants combined with the limited disclosure of the effect of CDKI1 and ICN2 expression in plants does not enable the full scope of the claimed invention given the breadth of the claims which encompass the use of nucleic acids encoding any type of cyclin-dependent kinase inhibitor polypeptide obtained from any plant species and the use of heterologous nucleic acids encoding any type of cyclin-dependent kinase inhibitor polypeptide obtained from any organism for the purpose of inhibiting any

unspecified aspect of development in any unspecified differentiated plant tissue, and given the unpredictability of using such nucleic acids to specifically modify the development of a plant transformed therewith as set forth above.

Claim Rejections - 35 USC § 102

Claims 1, 8, 9, 15, and 18 and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by John (U.S. Patent Number 5, 750, 862, May 12, 1998), for the reasons of record set forth in the office action mailed November 5, 2003.

Applicant's arguments filed September 7, 2004, have been fully considered but they are not persuasive.

Applicants note that in column 4, lines 57-58, the cited patent identifies the WEE-1 and MIK-1 genes as being from the fission yeast. Applicants also note that the Examiner asserts that the yeast WEE-1 or MIK-1 polypeptide would inhibit a plant CDK, and Applicants submit that there is no evidence to support this assertion. Applicants further maintain that the sequences of the yeast CDK inhibitors lack the requisite homology with the plant CDK inhibitor consensus sequence. Applicants accordingly maintain that these are not plant CDK inhibitors, and the reference cannot anticipate the present claims. (brief page 13)

With respect to Applicants' observation that the cited patent identifies the WEE-1 and MIK-1 genes as being from the fission yeast, the Examiner notes that rejected claims 15 and 18 do not exclude genes obtained from yeast, as claims 15 and 18 require only "a heterologous nucleic acid encoding a cyclin-dependent kinase inhibitor". Additionally, the specification at page 10 discloses that "A CDK inhibitor polypeptide is any

polypeptide capable of inhibiting a CDK" (lines 24-25), and at page 15 the specification discloses that the term cyclin-dependent kinase inhibitor includes "any polypeptide capable of functioning to inhibit a cyclin-dependent kinase" (lines17-21).

With respect to Applicants' assertion that there is no evidence to support the Examiner's assertion that the yeast WEE-1 or MIK-1 polypeptide would inhibit a plant CDK, the Examiner maintains that because the claims of an issued patent are presumed valid, it is presumed that the yeast WEE-1 or MIK-1 polypeptide would inhibit a plant CDK in the transgenic plants claimed in this patent, since the claimed plants may be transformed with only one of a coding sequence for the yeast WEE-1 or MIK-1 polypeptide, and since WEE-I and MIK-I are known to function by inhibiting the activity of cyclin-dependent kinases.

In this regard the Examiner further notes that a second patent, U.S. Patent No. 6,087,175, issued July 11, 2000 as a continuation of the parent (application no. 08/066,092) of U.S. Patent Number 5,750, 862. The '175 patent additionally claims, on the basis of an identical disclosure, methods that require modulating the level and/or catalytic activity of at least one of a cell cycle control protein in a plant, including a cyclin-dependent inhibitor polypeptide (WEE-1 or MIK-1), for the purpose of controlling plant cell growth, maintaining, enhancing or otherwise facilitating plant cell division, enhancing or promoting regeneration of a plant, modifying plant growth behavior, and regenerating a plant. Because the claims of the '175 patent are presumed valid, it is presumed that the yeast WEE-1 or MIK-1 polypeptide would inhibit a plant CDK in the methods claimed in this patent, since the claimed methods require that modulating the level and/or catalytic activity of at least one of a cell cycle control protein, including a

cyclin-dependent inhibitor polypeptide (WEE-1 or MIK-1), in a plant result in the control plant cell growth, the maintenance, enhancement or facilitation of plant cell division, the enhancement or promotion of the regeneration of a plant, the modification of plant growth behavior, and the regeneration of a plant, and since WEE-1 and MIK-1 are known to function by inhibiting the activity of cyclin-dependent kinases.

With respect to Applicants' assertion that the sequences of the yeast CDK inhibitors lack the requisite homology with the plant CDK inhibitor consensus sequence, the Examiner maintains that the rejected claims impose no requirement whatsoever for any type or for any amount of homology with any plant CDK inhibitor consensus sequence.

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Cynthia Collins whose telephone number is (571) 272-0794. The examiner can normally be reached on Monday-Friday 8:45 AM -5:15 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson can be reached on (571) 272-0804. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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